UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,929	04/16/2004	Alexander Lai	57657/04-265	1334

22206 7590 03/08/2005

FELLERS SNIDER BLANKENSHIP
BAILEY & TIPPENS
THE KENNEDY BUILDING
321 SOUTH BOSTON SUITE 800
TULSA, OK 74103-3318

EXAMINER	
MCGAW, MICHAEL M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,929	LAI, ALEXANDER	
	Examiner	Art Unit	
	Michael M. McGaw	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *25 Oct 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment Prinout*.

DETAILED ACTION

This is the first action on the merits for Application 10/826,929. Claims 1-19 are currently pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3, 6, 11 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 states "wherein the HA1 encoding sequence is ***for*** strain A/Eq/Kentucky/98." (emphasis added) Does Applicant mean "wherein the HA1 encoding sequence is ***from*** strain A/Eq/Kentucky/98" or is Applicant specifying that the vaccine is intended only against strain A/Eq/Kentucky/98? In the interest of compact prosecution the Examiner is interpreting the claim as specifying that the encoding sequence is from A/Eq/Kentucky/98 and would be more broadly applicable than a vaccine that is only specific for strain A/Eq/Kentucky/98. Such treatment does not relieve applicant of a response to this rejection. Appropriate correction is required.

Claim 6 states in relevant part "further comprising a vector ***for containing*** the HA1 encoding sequence." (emphasis added) It is unclear what is meant by the emphasized phrase. It appears to the Examiner that the word "for" was inadvertently included in the sentence. In the interest of compact prosecution the Examiner is

interpreting the claim without this word. Such treatment does not relieve applicant of a response to this rejection. Appropriate correction is required.

Claim 17 states "[t]he method according to claim 15, wherein the vector is a liposome." Claim 15 specifies that the vector is a eukaryotic vector. Stedman's Medical Dictionary, 27th Edition defines liposome as "[a]ny small, roughly spherical artificial vesicle consisting of a lipid bilayer enclosing some of the suspending medium." Vectors are variously defined Stedman's Medical Dictionary, 27th Edition including the definition for expression vector as "[a] plasmid, yeast or animal virus genome used experimentally to introduce foreign genetic material into a propagatable host cell in order to replicate and amplify the foreign DNA sequences as a recombinant molecule." The point being that liposomes are not vectors. They may contain vectors, but they might instead contain something else such as an immunogenic protein. Moreover, while vectors such as certain plasmids can be described as eukaryotic or prokaryotic, the term is meaningless in reference to a liposome.

Claim 11 contains the trademark/trade name METASTIM. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the

present case, the trademark/trade name is used to identify/describe the adjuvant and, accordingly, the identification/description is indefinite.

Claim 14 is generally directed at a method of inducing an immune response (i.e. a method of using), but includes the step of inserting the HA1 encoding sequence into a vector (a step directed at a method of making rather than using). The Examiner is interpreting this method of inducing an immune response as ***requiring*** the step of inserting the HA1 coding sequence into the vector. This is not a rejection but is merely intended to set forth how the Examiner is interpreting the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 6-7 rejected under 35 U.S.C. 102(b) as being anticipated by Olsen, C.W. et al. (1997) Vaccine, 15(10):1149-1156 ("Olsen").

Applicant claims "[a] vaccine for equine influenza virus, comprising an effective immunizing amount of an isolated DNA, the isolated DNA comprising an HA1 encoding sequence of a strain of equine-2 influenza virus, and a pharmacologically acceptable carrier or diluent."

Olsen teaches nucleic acid vaccines for equine influenza virus utilizing the full-length HA gene from the equine-2 influenza strain A/Equine/Kentucky/1/81. (See page 1150, Materials and Methods) Applicant has indicated "the isolated DNA ***comprising*** an HA1 encoding sequence of a strain of equine-2 influenza virus..." (emphasis added) Therefore Applicant claims an isolated DNA that includes the HA1 encoding region, but may include other unspecified elements as well. (See MPEP 2111.02) As the gene used by Olsen was the full-length HA gene, this would include the HA1 coding sequence. The DNA vaccine plasmid expressing the HA from A/Equine/Kentucky/1/81 was cloned into the eukaryotic expression vector pWGR and used the immediate early promoter from CMV.

Claims 1-2, 6-7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Larsen, D.L. et al. (1998) *J. Virol.* 72(2):1704-8 ("Larsen").

Larsen teaches the coadministration of plasmid DNA encoding the cytokine/adjuvant IL-6 with plasmids encoding the HA gene from the equine-2 influenza strain A/Equine/Kentucky/1/81. (See page 1705). Larsen utilized the nucleic acid vaccine of Olsen, which is described more fully immediately above. Expressed IL-6 gene would constitute a peptide adjuvant within the scope of claim 10.

Claims 1-2, 6-7 and 13 rejected under 35 U.S.C. 102(b) as being anticipated by Lunn, D.P. et al. (1999) Vaccine, 17:2245-2258 ("Lunn").

Lunn teaches nucleic acid vaccines for equine influenza virus and methods of inducing an immune response against equine influenza virus via administration to an equid an effective amount of the aforementioned nucleic acid vaccine. (See page 2247) Lunn utilized the nucleic acid vaccine of Olsen, which is described more fully above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen, C.W. et al. (1997) *Vaccine,* 15(10):1149-1156 ("Olsen") as applied to claims 1-2 and 6-7 above, and further in view of Lai, A.C.K. et al. Arch Virol. 2001;146(6):1063-74 ("Lai") (cited by Applicant).

Olsen is as discussed above. Olsen's construct utilized the HA1 coding region from A/Eq/Kentucky/81. Thus, Olsen does not teach the HA1 encoding sequence from A/Eq/Kentucky/98.

Lai teaches the HA1 encoding sequence from A/Eq/Kentucky/98. Table 1 of Lai provides sequence accession numbers for the HA1 segments including the accession number for the HA1 sequence for A/Eq/Kentucky/98. The "Sequence Alignment Printout" included with this Office Action shows the alignment of SEQ ID NO. 1 which has 100% sequence identity to the sequence disclosed by Lai. One of ordinary skill in

the art would have been motivated to substitute the HA gene sequence from A/Eq/Kentucky/81 as taught by Olsen with the HA gene sequence of A/Eq/Kentucky/98 as taught by Lai because A/Eq/Kentucky/98 represents a current isolate which is more indicative of currently circulating equine influenza viruses and thus more likely to be encountered. One of ordinary skill in the art would have expected a DNA vaccine against equine influenza based upon the HA1 gene of A/Eq/Kentucky/98 that protects against currently circulating strains because Olsen teaches the efficacy of DNA vaccines against equine influenza viruses using the HA gene while Lai teaches the sequence of A/Eq/Kentucky/98 and its relevance to currently circulating equine influenza. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen, C.W. et al. (1997) *Vaccine,* 15(10):1149-1156 ("Olsen") as applied to claims 1-2 and 6-7 above, and further in view of Chen, Z. et al. (1999) *Vaccine*, 17(7-8):653-9 ("Chen").

Olsen is as discussed above. Olsen does not teach additional encoding sequences encoding additional antigenic components beyond the HA gene of influenza virus.

Chen teaches nucleic acid vaccines for influenza virus encoding sequences for additional antigenic components beyond the HA antigen. Chen was working with human influenza virus strains and used gene segments from A/PR/8/34. (See page 654, col. 1, Materials and Methods). Chen teaches that vaccines composed of mixtures of plasmid

DNAs encoding HA and NA induced more enhanced protection against influenza virus challenge than either of the plasmids administered alone. (See page 658, Discussion) Chen further teaches that such a mixture of viral protein-expressing plasmid DNAs helps provide protection against heterologous virus infection. One of ordinary skill in the art would have been motivated to add because additional encoding sequences for additional antigenic components because Chen teaches that such vaccines confer additional protection against homologous challenge and also help protect against heterologous challenge. One of ordinary skill in the art would have expected broader protection by adding additional antigen encoding sequences because such additional sequences would be expected to stimulate immunity against additional antigenic features of the influenza virus. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen, C.W. et al. (1997) *Vaccine,* 15(10):1149-1156 ("Olsen") as applied to claims 1-2 and 6-7 above, and further in view of the Invitrogen Catalog ("Invitrogen")(as found on the Invitrogen website and cited on Form 892).

Olsen is as taught above. Olsen does not teach pcDNA3.1/V5-His-TOPO. pcDNA3.1/V5-His-TOPO is a widely used, commercially available DNA vector as evidenced by the printout from Invitrogen. Invitrogen teaches that the vector offers a strong CMV promoter for high-level, constitutive expression in mammalian cells. Numerous citations to documents evidencing use of this plasmid are shown in the lower

right portion of the supplied Invitrogen document, including a reference in *Mol Cell Biol.* to Kasoff et al (see also form 892) evidencing the availability of this vector back as far as 1999. One of ordinary skill in the art would have been motivated to combine the teachings of Olsen with use of the Invitrogen vector as Invitrogen teaches the ease of use of the pcDNA3.1/V5-His-TOPO vector and its high-level, constitutive expression in mammalian cells. One of ordinary skill in the art would have expected an efficacious DNA vaccine based upon an HA insert in the pcDNA3.1/V5-His-TOPO vector because genes, vectors and techniques were all well-characterized at the time of Applicant's invention as evidenced by the combined teachings of Olsen and Invitrogen. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 12, 14-15 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lunn, D.P. et al. (1999) Vaccine, 17:2245-2258 ("Lunn") as applied to claims 1-2, 6-7 and 13 above, and further in view of Wong, J.P. et al. Vaccine. 2001 Mar 21;19(17-19):2461-7. ("Wong").

Lunn is as discussed above. Lunn teaches the step of inserting the HA1 encoding sequence into a eukaryotic vector. (See also Olsen, above) Lunn teaches the administration of the vaccine to the mucosal surfaces via gene gun administration. Lunn does not teach the intranasal administration of the vaccine into the respiratory tract. Lunn does not teach delivery in a liposome.

Wong teaches delivering the vaccine intranasally into the respiratory tract. (see paragraph spanning pages 2462-2463) Wong delivered the DNA with and without encapsulation in liposomes. (See page 2462, col. 2 for a discussion on the liposome encapsulation procedure). Wong teaches that the delivery of 50 μl of 0.4 mg/ml of the DNA preparation in the intranasal challenge. (see page 2463, col. 1) Without knowing the weight of the mice, etc., it is not clear whether this falls within the ranges specified in claims 18 and 19. Nevertheless, it would have been obvious to one skilled in the art at the time of invention to determine all operable and optimum component ratios/concentrations in the compositions as taught by Lunn and/or Wong, because the component ratios/concentrations are an art-recognized result-effective variable that is routinely determined and optimized in the vaccine arts. On page 2466 Wong teaches:

> When plasmid DNA is administered into the respiratory tract, liposomes can facilitate the uptake/transport of the plasmid DNA into the induction and effector sites ... The delivery of the plasmid DNA by liposomes to these sites can result in the induction of protective mucosal immunity in the mucosal surfaces in the respiratory tract. This may account for the observation that liposome-encapsulated pCI-HA10 in this present study induced a strong mucosal IgA response when it is administered into the respiratory tract but did not when injected directly into the muscles. Similarly, i.n. immunization with naked pCI-HA10 did not elicit any detectable mucosal IgA response. The inability of i.n. immunization with naked plasmid DNA to induce mucosal immunity is also reported by others [2]. These findings support the importance of using liposomes as vaccine carriers to the mucosal surfaces. The mucosal surface in respiratory tract is large and represents the primary site of entry and infection for many respiratory pathogens including influenza. Development of a DNA immunization strategy that could induce protective mucosal immunity can be valuable in reducing morbidity and mortality associated with infections caused by these pathogens. Mucosal vaccination using liposome-encapsulated plasmid DNA could also be very important in eliciting protective immunity at sites distant from the site of vaccine administration.

Thus, Wong teaches the importance of intranasal administration to induce a strong mucosal IgA response at the primary site of entry and infection of influenza. Moreover, Wong teaches that intranasal immunization of influenza DNA vaccines should include liposome encapsulation of the DNA as evidenced by the superior results achieved with

liposome-encapsulated nucleic acid relative to "naked" DNA. One of ordinary skill in the art would have been motivated to add/combine the teachings of Lunn with those of Wong because Wong teaches the efficacy of intranasal administration of liposome encapsulated DNA vaccines against influenza HA and Wong teaches that such an administration strategy induces mucosal immunity at the primary site of infection. One of ordinary skill in the art would have expected to achieve a liposome-encapsulated intranasal vaccine against equine influenza HA because the required techniques were well-developed and provided in the combined teachings of Lunn and Wong. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lunn, D.P. et al. (1999) Vaccine, 17:2245-2258 ("Lunn") in view of Wong, J.P. et al. Vaccine. 2001 Mar 21;19(17-19):2461-7 ("Wong") as applied to claims 12, 14-15 and 17-19 above, and further in view of the Invitrogen Catalog ("Invitrogen")(as found on the Invitrogen website and cited on Form 892).

This rejection involves identical reasoning to that applied to the rejection of claim 8 above under 35 U.S.C. 103(a) to Olsen in view of Invitrogen and therefore is not repeated in the present rejection. Lunn in view of Wong supplies the method steps of inducing an immune response against to an equid which are missing in the teachings of Olsen as used in the rejection of claim 8.

Conclusion

All claims are rejected. No claims are deemed free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael M. McGaw whose telephone number is (571) 272-2902. The examiner can normally be reached on Monday through Friday from 8 A.M. to 5 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. M.

Michael M. McGaw
Tuesday, March 01, 2005

James C. Housel 3/7/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Sequence Alignment Printout

SEQ ID NO:1

GenCore version 5.1.6

OM nucleic - nudleic search, using sw model

Run on: March 1, 2005, 01:45:21 ; Search time 4887 Seconds
(without alignments)
10519.948 Million cell updates/sec

Title: US-10-826-929A-1
Perfect score: 1061
Sequence: 1 agcaaaagcaggggatattt.....taccagaaaagcaaatcaga 1061

Scoring table: IDENTITY_NUC
Gapop 10.0 , Gapext 1.0

Searched: 4708233 seqs, 24227607955 residues

Total number of hits satisfying chosen parameters: 9416466

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : GenEmbl:*
1: gb_ba:*
2: gb_htg:*
3: gb_in:*
4: gb_om:*
5: gb_ov:*
6: gb_pat:*
7: gb_ph:*
8: gb_pl:*
9: gb_pr:*
10: gb_ro:*
11: gb_sts:*
12: gb_sy:*
13: gb_un:*
14: gb_vi:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1061	100.0	1061	14	AF197241	AF197241 Influenza
2	1056.2	99.5	1061	14	AY273168	AY273168 Influenza
3	1053	99.2	1061	14	AF197248	AF197248 Influenza
4	1051.4	99.1	1061	14	AF197247	AF197247 Influenza
5	1048.2	98.8	1762	14	FLAHAH3B	L39914 Influenza A
6	1043.4	98.3	1060	14	EIVY14059	Y14059 Influenza A
7	1041.8	98.2	1060	14	EIVY14060	Y14060 Influenza A
8	1041.8	98.2	1762	14	FLAHAH3D	L39916 Influenza A
9	1039.2	97.9	1100	14	EIVY14058	Y14058 Influenza A
10	1038.6	97.9	1762	14	FLAHAH3F	L39918 Influenza A
11	1035.4	97.6	1061	14	AF197242	AF197242 Influenza
12	1033.8	97.4	1762	6	BD244631	BD244631 Low tempe
13	1033.8	97.4	1762	6	AR254631	AR254631 Sequence
14	1033.8	97.4	1762	6	AR343239	AR343239 Sequence
15	1033.8	97.4	1762	6	AR455506	AR455506 Sequence
16	1033.8	97.4	1762	14	FLAHAH3A	L39913 Influenza A
17	1032.2	97.3	1762	6	BD244629	BD244629 Low tempe
18	1032.2	97.3	1762	6	AR254629	AR254629 Sequence
19	1032.2	97.3	1762	6	AR343237	AR343237 Sequence
20	1032.2	97.3	1762	6	AR455504	AR455504 Sequence
21	1030.6	97.1	1061	14	AF197245	AF197245 Influenza
22	1030.6	97.1	1762	14	FLAHAH3E	L39917 Influenza A
23	1029	97.0	1061	14	AF197249	AF197249 Influenza
24	1027.4	96.8	1762	14	FLAHAH3C	L39915 Influenza A
25	1022.6	96.4	1061	14	AF197243	AF197243 Influenza
26	1022.6	96.4	1061	14	AF197244	AF197244 Influenza
27	1022.6	96.4	1090	14	EIVY14056	Y14056 Influenza A
28	1022.6	96.4	1762	14	IVAH691	X95637 Influenza A
29	1021.2	96.2	1762	14	IVAH991	X95638 Influenza A
30	1019.4	96.1	1061	14	AY273167	AY273167 Influenza
31	1019.2	96.1	1032	14	IVTAN931	X85088 Influenza A
32	1019.2	96.1	1698	6	AR490205	AR490205 Sequence
33	1019.2	96.1	1698	6	AX018718	AX018718 Sequence
34	1018.4	96.0	1762	6	AR011427	AR011427 Sequence
35	1018.4	96.0	1762	6	I18065	I18065 Sequence 30
36	1016.8	95.8	1762	14	FLAET85HA	M24726 Influenza A
37	1016.2	95.8	1762	14	EIVH3A	L27597 Influenza A
38	1015.6	95.7	1040	14	FLAH3N8HAD	D30680 Influenza A
39	1014.6	95.6	1061	14	AF197246	AF197246 Influenza
40	1014.2	95.6	1099	14	FLAH3N8HAJ	D30686 Influenza A
41	1011.8	95.4	1093	14	FLAH3N8HAE	D30681 Influenza A
42	1010.4	95.2	1762	14	FLAEK87HA	M24728 Influenza A
43	1008.8	95.1	1762	14	FLAEK86HA	M24727 Influenza A
44	1007	94.9	1096	14	FLAH3N8HAG	D30683 Influenza A
45	1006.6	94.9	1060	14	EIVY14057	Y14057 Influenza A

ALIGNMENTS

RESULT 1
AF197241
LOCUS AF197241 1061 bp mRNA linear VRL 08-JAN-2003
DEFINITION Influenza A virus (A/equine/Kentucky/1/98(H3N8)) hemagglutinin precursor (HA1) mRNA, partial cds.
ACCESSION AF197241
VERSION AF197241.1 GI:6651502
KEYWORDS .
SOURCE Influenza A virus (A/equine/Kentucky/1/98(H3N8))
ORGANISM Influenza A virus (A/equine/Kentucky/1/98(H3N8))
Viruses; ssRNA negative-strand viruses; Orthomyxoviridae; Influenzavirus A.
REFERENCE 1 (bases 1 to 1061)
AUTHORS Lai,A.C., Chambers,T.M., Holland,R.E. Jr., Morley,P.S., Haines,D.M., Townsend,H.G. and Barrandeguy,M.
TITLE Diverged evolution of recent equine-2 influenza (H3N8) viruses in the Western Hemisphere
JOURNAL Arch. Virol. 146 (6), 1063-1074 (2001)
MEDLINE 21395169
PUBMED 11504416
REFERENCE 2 (bases 1 to 1061)
AUTHORS Lai,A.C.K.
TITLE Direct Submission
JOURNAL Submitted (21-OCT-1999) Microbiology & Molecular Genetics, Oklahoma State University, 306 Life Science East, Stillwater, OK 74078, USA

FEATURES	Location/Qualifiers
source	1. .1061
	/organism="Influenza A virus (A/equine/Kentucky/1/98(H3N8))"
	/virion
	/mol_type="mRNA"
	/isolate="A/equine/Kentucky/1/98"
	/db_xref="taxon:217817"
	/note="H3N8"
gene	1. .>1061
	/gene="HA1"
CDS	30. .>1061
	/gene="HA1"
	/codon_start=1
	/product="hemagglutinin precursor"
	/protein_id="AAF22345.1"
	/db_xref="GI:6651503"

```
                     /translation="MKTTIILILLLTHWVYSQNPTSGNNTATLCLGHHAVANGTLVKTI
                     TDDQIEVTNATELVQSISIGKICNNSYKVLDGRNCTLIDAMLGDPHCDVFQYENWDLF
                     IERSSAFSNCYPYDIPDYASLRSIVASSGTLEFTAEGFTWTGVTQNGRSGACKRGSAD
                     SFFSRLNWLTKSGNSYPTLNVTMPNNKNFDKLYIWGIHHPSSNQQQTELYIQESGRVT
                     VSTKRSQQTIVPNIGSRPWVRGQSGRISIYWTIVKPGDILMINSNGNLVAPRGYFKLK
                     TGKSSVMRSDAPIDICVSECITPNGSIPNDKPFQNVNKVTYGKCPKYIRQNTLKLATG
                     MRNIPEKQIR"
     sig_peptide     30. .74
                     /gene="HA1"
     mat_peptide     75. .>1061
                     /gene="HA1"
                     /product="hemagglutinin"
ORIGIN

  Query Match          100.0%;  Score 1061;  DB 14;  Length 1061;
  Best Local Similarity  100.0%;  Pred. No. 8.3e-242;
  Matches 1061;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 AGCAAAAGCAGGGGATATTTCTGTCAATCATGAAGACAACCATTATTTTGATACTACTGA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 AGCAAAAGCAGGGGATATTTCTGTCAATCATGAAGACAACCATTATTTTGATACTACTGA 60

Qy         61 CCCATTGGGTCTACAGTCAAAACCCAACCAGTGGAAACAACACAGCCACATTATGTCTGG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 CCCATTGGGTCTACAGTCAAAACCCAACCAGTGGAAACAACACAGCCACATTATGTCTGG 120

Qy        121 GACACCATGCAGTAGCAAATGGAACATTGGTAAAAACAATAACTGATGACCAAATTGAGG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GACACCATGCAGTAGCAAATGGAACATTGGTAAAAACAATAACTGATGACCAAATTGAGG 180

Qy        181 TGACAAATGCTACTGAATTAGTTCAGAGCATTTCAATAGGGAAAATATGCAACAACTCAT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TGACAAATGCTACTGAATTAGTTCAGAGCATTTCAATAGGGAAAATATGCAACAACTCAT 240

Qy        241 ATAAAGTTCTAGATGGAAGAAATTGCACATTAATAGATGCAATGCTAGGAGACCCCCACT 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ATAAAGTTCTAGATGGAAGAAATTGCACATTAATAGATGCAATGCTAGGAGACCCCCACT 300

Qy        301 GTGATGTCTTCCAGTATGAGAATTGGGACCTCTTCATAGAAAGAAGCAGCGCTTTCAGCA 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GTGATGTCTTCCAGTATGAGAATTGGGACCTCTTCATAGAAAGAAGCAGCGCTTTCAGCA 360

Qy        361 ATTGCTACCCATATGACATCCCTGACTATGCATCGCTCCGGTCCATTGTAGCATCCTCAG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 ATTGCTACCCATATGACATCCCTGACTATGCATCGCTCCGGTCCATTGTAGCATCCTCAG 420

Qy        421 GAACATTAGAATTCACAGCAGAGGGATTCACATGGACAGGTGTCACTCAAAACGGAAGAA 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 GAACATTAGAATTCACAGCAGAGGGATTCACATGGACAGGTGTCACTCAAAACGGAAGAA 480

Qy        481 GTGGAGCCTGCAAAAGGGGATCAGCCGATAGTTTCTTTAGCCGACTGAATTGGCTAACAA 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 GTGGAGCCTGCAAAAGGGGATCAGCCGATAGTTTCTTTAGCCGACTGAATTGGCTAACAA 540

Qy        541 AATCTGGAAACTCTTACCCCACATTGAATGTGACAATGCCTAACAATAAAAATTTCGACA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 AATCTGGAAACTCTTACCCCACATTGAATGTGACAATGCCTAACAATAAAAATTTCGACA 600

Qy        601 AACTATACATCTGGGGGATTCATCACCCGAGCTCAAACCAACAGCAGACAGAATTGTACA 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 AACTATACATCTGGGGGATTCATCACCCGAGCTCAAACCAACAGCAGACAGAATTGTACA 660

Qy        661 TCCAAGAATCAGGACGAGTAACAGTCTCAACAAAAAGAAGTCAACAAACGATAGTCCCTA 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 TCCAAGAATCAGGACGAGTAACAGTCTCAACAAAAAGAAGTCAACAAACGATAGTCCCTA 720

Qy        721 ATATCGGATCTAGACCGTGGGTTAGGGGTCAATCAGGCAGGATAAGCATATACTGGACCA 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 ATATCGGATCTAGACCGTGGGTTAGGGGTCAATCAGGCAGGATAAGCATATACTGGACCA 780

Qy        781 TTGTAAAACCTGGAGATATCCTAATGATAAACAGTAATGGCAACTTAGTTGCACCGCGGG 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TTGTAAAACCTGGAGATATCCTAATGATAAACAGTAATGGCAACTTAGTTGCACCGCGGG 840

Qy        841 GATATTTTAAATTGAAAACAGGGAAAAGCTCTGTAATGAGATCAGATGCACCCATAGACA 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 GATATTTTAAATTGAAAACAGGGAAAAGCTCTGTAATGAGATCAGATGCACCCATAGACA 900

Qy        901 TTTGTGTGTCTGAATGTATTACACCAAATGGAAGCATCCCCAACGACAAACCATTTCAAA 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TTTGTGTGTCTGAATGTATTACACCAAATGGAAGCATCCCCAACGACAAACCATTTCAAA 960

Qy        961 ATGTGAACAAAGTTACATATGGAAAATGCCCCAAGTATATCAGGCAAAACACTTTAAAGC 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ATGTGAACAAAGTTACATATGGAAAATGCCCCAAGTATATCAGGCAAAACACTTTAAAGC 1020

Qy       1021 TGGCCACTGGGATGAGGAATATACCAGAAAAGCAAATCAGA 1061
              |||||||||||||||||||||||||||||||||||||||||
Db       1021 TGGCCACTGGGATGAGGAATATACCAGAAAAGCAAATCAGA 1061
```

```
RESULT 2
AY273168
LOCUS       AY273168               1061 bp    RNA     linear   VRL 19-MAR-2004
DEFINITION  Influenza A virus (A/equine/Oklahoma/2000(H3N8)) hemagglutinin
            precursor (HA1) gene, partial cds.
ACCESSION   AY273168
VERSION     AY273168.1  GI:33415851
KEYWORDS    .
SOURCE      Influenza A virus (A/equine/Oklahoma/2000(H3N8))
  ORGANISM  Influenza A virus (A/equine/Oklahoma/2000(H3N8))
            Viruses; ssRNA negative-strand viruses; Orthomyxoviridae;
            Influenzavirus A.
REFERENCE   1  (bases 1 to 1061)
  AUTHORS   Lai,A.C.K., Rogers,K.M., Glaser,A., Tudor,L. and Chambers,T.
  TITLE     Alternate circulation of recent equine-2 influenza viruses (H3N8)
            from two distinct lineages in the United States
  JOURNAL   Virus Res. 100 (2), 159-164 (2004)
   PUBMED   15019234
REFERENCE   2  (bases 1 to 1061)
  AUTHORS   Lai,A.C.K.
  TITLE     Direct Submission
  JOURNAL   Submitted (10-APR-2003) Microbiology & Molecular Genetics, Oklahoma
            State University, 306 Life Science East, Stillwater, OK 74078, USA
FEATURES             Location/Qualifiers
     source          1. .1061
                     /organism="Influenza A virus
                     (A/equine/Oklahoma/2000(H3N8))"
                     /virion
                     /mol_type="genomic RNA"
                     /isolate="A/Eq/Oklahoma/2000"
                     /db_xref="taxon:241186"
     gene            30. .>1061
                     /gene="HA1"
     CDS             30. .>1061
                     /gene="HA1"
                     /codon_start=1
                     /product="hemagglutinin precursor"
                     /protein_id="AAQ18435.1"
                     /db_xref="GI:33415852"
                     /translation="MKTTIILILLTHWVYSQNPTSGNNTATLCLGHHAVANGTLVKTI
                     TDDQIEVTNATELVQSISIGKICNNSYKVLDGRNCTLIDAMLGDPHCDVFQYENWDLF
                     IERSSAFSNCYPYDIPDYASLRSIVASSGTLEFTAEGFTWTGVTQNGRSGACKRGSAD
                     SFFSRLNWLTKSGNSYPTLNVTMPNNKNFDKLYIWGIHHPSSNQQQTELYIQESGRVT
                     VSTKRSQQTIVPNIGSRPWVRGQSGRISIYWTIVKPGDILMINSNGNLVAPRGYFKLK
                     TGESSVMRSDAPIDICVSECITPNGSIPNDKPFQNVNKVTYGKCPKYIRQNTLKLATG
                     MRNIPEKQIR"
ORIGIN

  Query Match          99.5%;  Score 1056.2;  DB 14;  Length 1061;
  Best Local Similarity  99.7%;  Pred. No. 1.2e-240;
  Matches 1058;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 AGCAAAAGCAGGGGATATTTCTGTCAATCATGAAGACAACCATTATTTTGATACTACTGA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 AGCAAAAGCAGGGGATATTTCTGTCAATCATGAAGACAACCATTATTTTGATACTACTGA 60
```